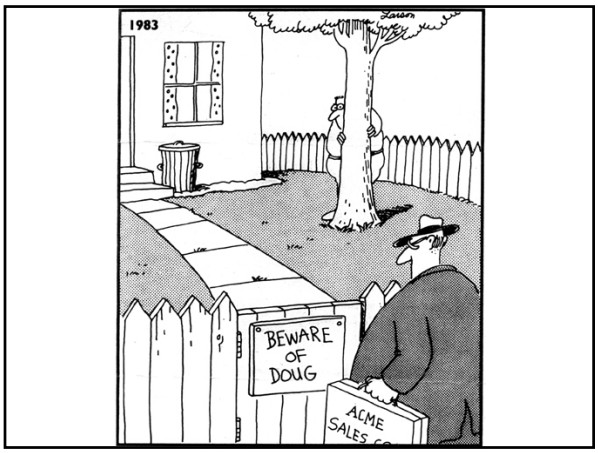


Current Concepts in the Diagnosis and Treatment of Diabetic Retinopathy

October 18, 2006

Douglas Mehr, MD
Rocky Mountain Retina Consultants
Salt Lake City, Utah

Epidemiology

18 million adults in United States
30% undiagnosed
WHO: 4% 1995 to 5.4% in 2025
Developed countries: 6.0% to 7.6%
24,000 become legally blind each year
5,000 cases of blindness

Epidemiology

DR leading cause of legal blindness in adults: 8% of cases
Over age 50: visual impairment
23.5% diabetics

Increased risk of glaucoma and cataracts

Cost to Society

$132 billion 2002 to $156 billion 2010
$192 billion in 2020
Diabetics spend >2.5x healthcare dollars
1997: $10,071 vs. $2669 per patient
$13,243 per capita 2002

Epidemiology

Diabetic retinopathy affects 50%

More than 5 million have DR
700,000 cases PDR annually

26% with DM for 25-50 years develop PDR
Type I greater risk than Type II

Impact on Patient

Unable to drive or read
Loss of employment/disability
Loss of independence
Depression

Loss of lower extremities, dialysis, MI, stroke, early death (leaving spouse and children)

Risk Factors

Obesity
Family history (genetic predisposition)
Smoking
Pregnancy

Systemic Problems

Diabetic retinopathy affects 50%

- Peripheral neuropathy (40%)
- Diabetic nephropathy (35%)
- Cardiovascular disease (43%)
- Hypertension (22% in Type I and 58% in Type II)
- Stroke
- Gastrointestinal complaints

Asymmetric disease

- Think carotid occlusive disease or vein occlusion.

Incidence of Diabetic Retinopathy

Duration of IDDM	Incidence of Retinopathy
5-7 years	50%
17-35 years	90%

Guidelines for Examinations

Age of onset of diabetes	First examination	Follow-up examinations
<30 years	5 yrs after diagnosis	Yearly
>30 years	At time of diagnosis	Yearly
Prior to pregnancy	Prior to conception or in the early first trimester.	Every 3 months

Differential Diagnosis

Hypertensive Retinopathy
Collagen vascular disease
HIV/AIDS
Cardiac embolic disease
Sickle-cell retinopathy
Radiation retinopathy
Vasculitis
Leukemia
Hepatitis

How Do We Approach
the Diabetic Patient?

What questions do we ask?

How do we address questions
the patient has?

What do we look for on examination?

How Do We Approach
the Diabetic Patient?

How is your vision?

Has your vision changed? In what way?

Is it bad enough to warrant intervention, i.e. cataract surgery, needle in eye, PPV, etc.?

How Do We Approach
the Diabetic Patient?

Do you take insulin?

What were your blood sugars this morning? Yesterday? Average?

How Do We Approach
the Diabetic Patient?

Do you take insulin?
Needed for diagnosis code and prognosis.

What were your blood sugars this morning? Yesterday? Average?

How Do We Approach
the Diabetic Patient?

Do you take insulin?
Needed for diagnosis code and prognosis.

What were your blood sugars this morning? Yesterday? Average?
Are they keeping tight control? Are they even monitoring? Do they need to see their internist?

How Do We Approach
the Diabetic Patient?

What is you current HgA1C?

What is your blood pressure?

How Do We Approach the Diabetic Patient?

What is you current HgA1C?
If the patient even knows what you're talking about, it's great news.

What is your blood pressure?

How Do We Approach the Diabetic Patient?

What is you current HgA1C?
If the patient even knows what you're talking about, it's great news.

What is your blood pressure?
Very important for macular edema.

Clinical Exam

Cornea: can I properly see the macula to assess and treat?

Iris: is there neovascularization?

Angle: gonioscopy for NVA.

Lens: is there a cataract present?

Vitreous: is there hemorrhage?

Clinical Exam

Optic nerve: NV? How many clock-hours?

Vessels: NVE, IRMA, venous-beading

Macula: exudates, IRH, MA, edema, CWS

Periphery: NVE? room for PRP?

Signs and Symptoms

Generalized Blurry Vision
- Cataract
- Macular edema
- Preretinal fibrosis
- Tractional retinal detachment

Floaters/Curtains/Blobs
- Vitreous Hemorrhage
- Combined rhegmatogenous-tractional retinal detachment

How Do We Approach the Diabetic Patient?

Make certain the patient understands that therapy is aimed at preserving the vision that remains.

Treatment goal: STABILIZATION

Bad retinopathy = poorer outcomes

How Do We Approach the Diabetic Patient?

If we do nothing, you will likely lose vision.

You MAY get vision back.

There are side effects from therapy but we are hoping to save central vision.

How Do We Approach the Diabetic Patient?

Photocoagulation:

- pain during and after procedure
- spots in vision
- loss of peripheral vision
- night blindness
- corneal abrasions/iris burns
- bleeding

How Do We Approach the Diabetic Patient?

Kenalog:

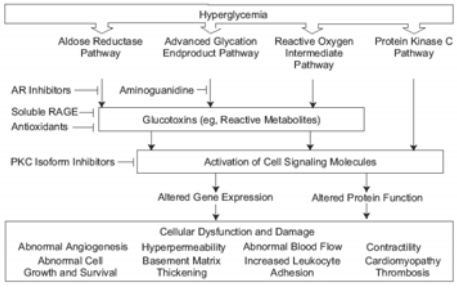
- FLOATERS
- cataract
- glaucoma
- endophthalmitis

How Do We Approach the Diabetic Patient?

Vitrectomy:

- pain and swelling
- bleeding
- high IOP
- cataract
- retinal detachment
- endophthalmitis

Pathogenesis



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Pathogenesis

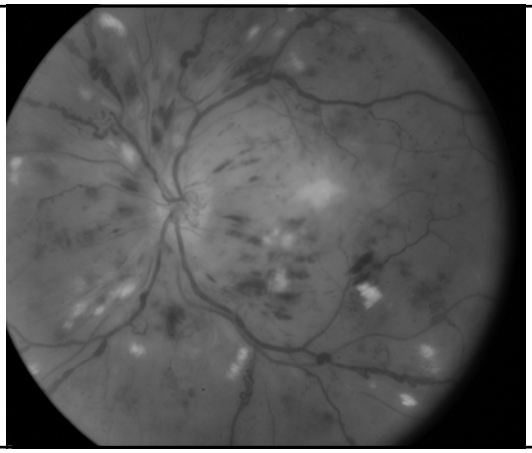
Hyperglycemia leads to cell wall dysfunction
→ vascular permeability
→ large proteins in extracellular matrix
→ oncotic forces
→ retinal edema and loss of vision

Pathogenesis

Subretinal exudates → fibrosis

Ischemia → permanent loss of vision

Vascular endothelial growth factor (VEGF) → neovascularization



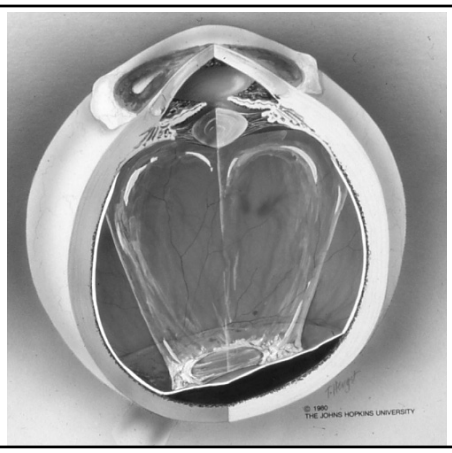
Pathogenesis

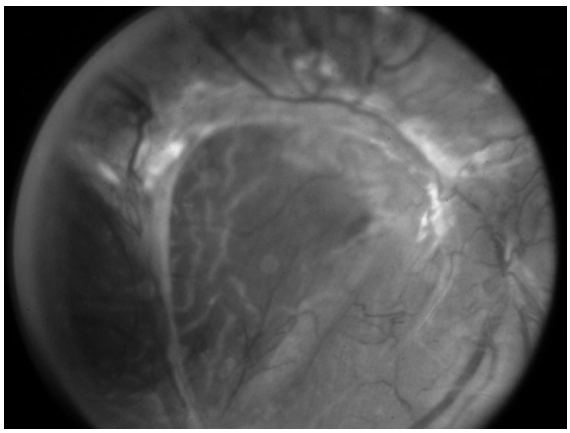
Continued cycle of new vessel growth and regression.

Fibrous tissue accompanies vascular growth.

Partial PVD and contraction of fibrous tissue pulls new vessels to cause VH.

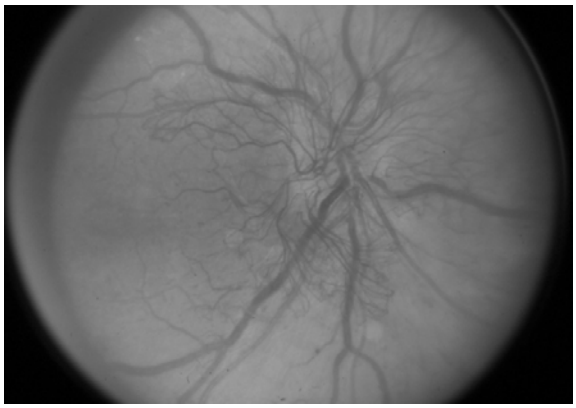
PVD spreads and cannot release causing TRD and macular drag.

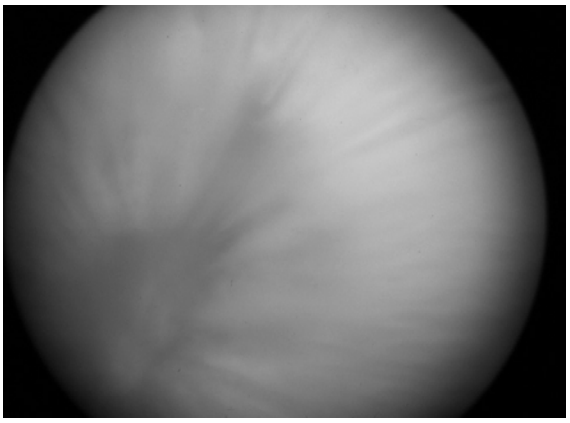




Pathogenesis

Neovascularization
→vitreous hemorrhage and tractional retinal detachments
→neovascular glaucoma → blind painful eye → enucleation





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Stages of Diabetic Retinopathy

No evidence of retinopathy
Mild non-proliferative diabetic retinopathy (NPDR)
Moderate NPDR
Severe/Very Severe NPDR
Proliferative diabetic retinopathy (PDR)

Stages of Diabetic Retinopathy

No evidence of retinopathy

Follow-up in one year

Stages of Diabetic Retinopathy

Mild non-proliferative diabetic retinopathy (NPDR)

Occasional microaneurysms

Follow-up in 12 months

Stages of Diabetic Retinopathy

Moderate NPDR

More microaneurysms and scattered hard exudates or cotton-wool spots.

Follow-up in 6-12 months.

Stages of Diabetic Retinopathy

Severe/Very Severe NPDR 4:2:1 rule

Four quadrants of severe retinal hemorrhages
Two quadrants of venous beading
One quadrant of moderately severe IRMA
(2 present = very severe)

Stages of Diabetic Retinopathy

Severe/Very Severe NPDR 4:2:1 rule

Follow-up 3-4 months

Stages of Diabetic Retinopathy

Proliferative diabetic retinopathy (PDR)

Need to decide if panretinal photocoagulation is necessary.

Stages of Diabetic Retinopathy

High-risk characteristics (from DRS):

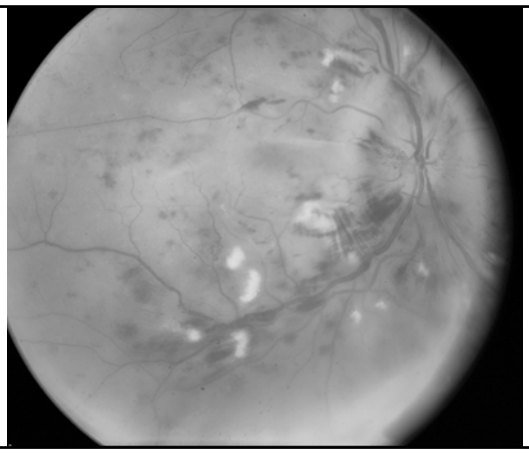
1. NVD, at least one-third of disc.
2. NVD on or within one disc diameter of the disc and vitreous or preretinal hemorrhage.
3. NVE, at least half of disc area and vitreous or preretinal hemorrhage.

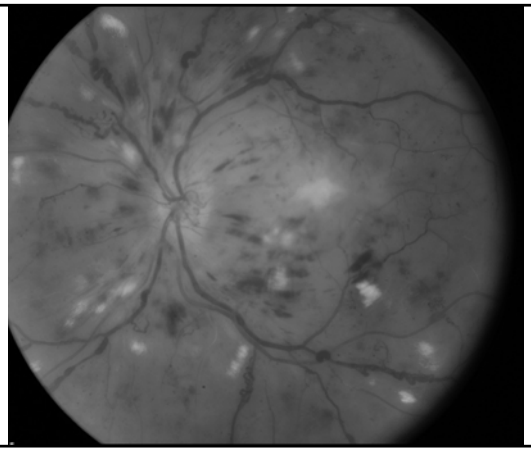
Stages of Diabetic Retinopathy

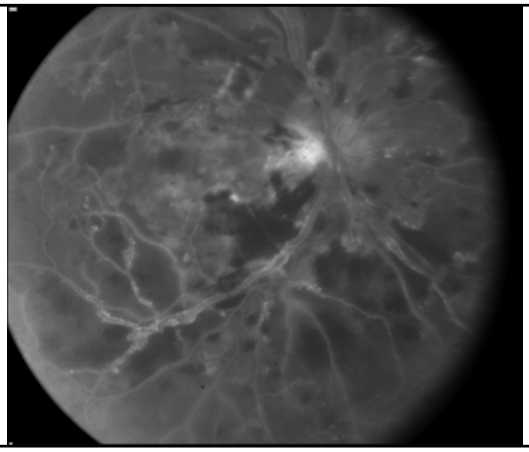
High-risk characteristics (from DRS):

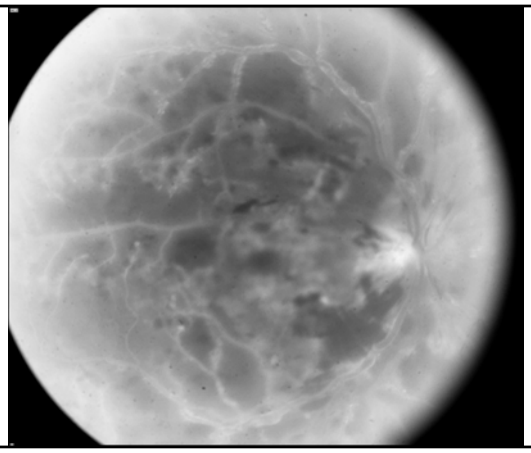
If present, proceed with PRP.

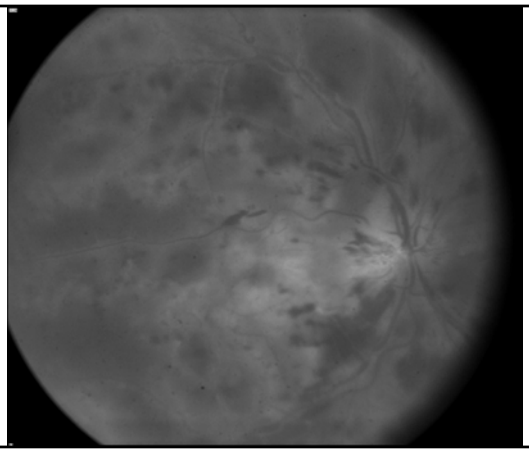
May initiate sooner for other concerns.











Laser Photocoagulation

Where to treat?
What kind of lens?
What wavelength?
Method of delivery (SL, LIO, OR)?
How often do we treat?

Not just a matter of “throw some laser in.”

Macular Edema

When is it clinically significant?

1. Thickening at or within 500 microns of FAZ.
2. Hard exudates at or within 500 microns of FAZ with associated thickening of adjacent retina.
3. A zone of retinal thickening one disc area or larger, any part of which is within one disc diameter of the center of the macula.

Laser Photocoagulation

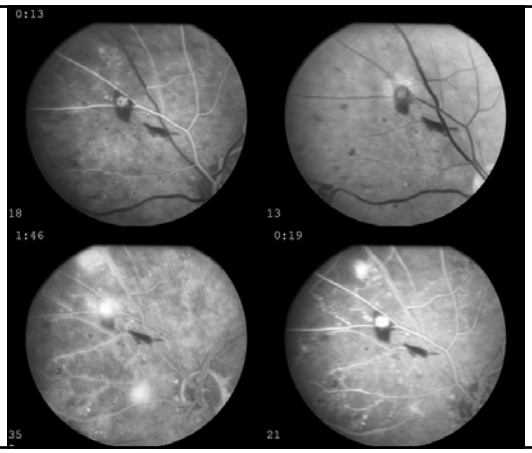
Where to treat?
What kind of lens?
What wavelength?
Method of delivery (SL, LIO, OR)?
How often do we treat?

Not just a matter of “throw some laser in.”

Ancillary Testing

Fluorescein angiogram
Optical Coherence Tomography (OCT)
Ultrasound
Fundus photos

Blood glucose
HgA1C
Blood pressure



Ancillary Testing

Fluorescein angiogram
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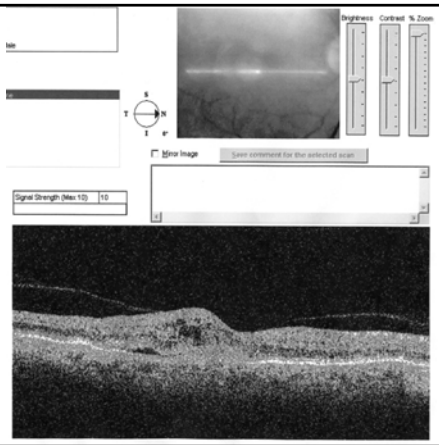

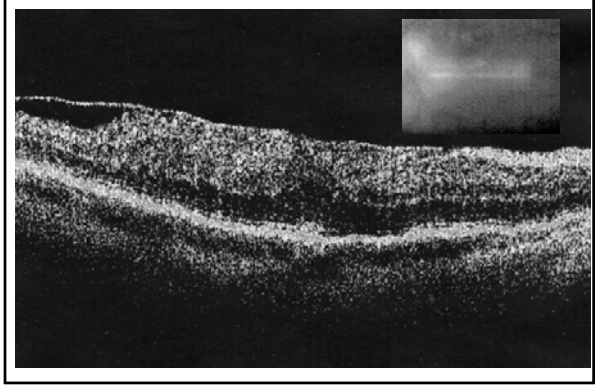

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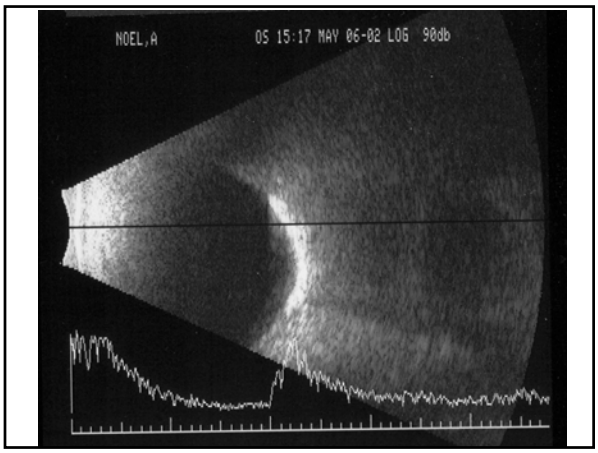

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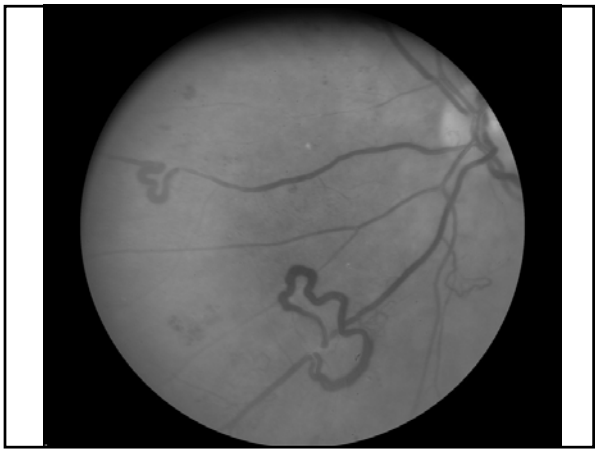
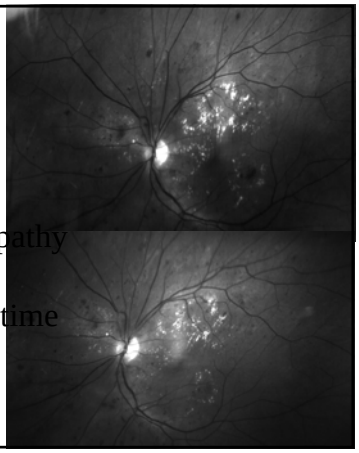
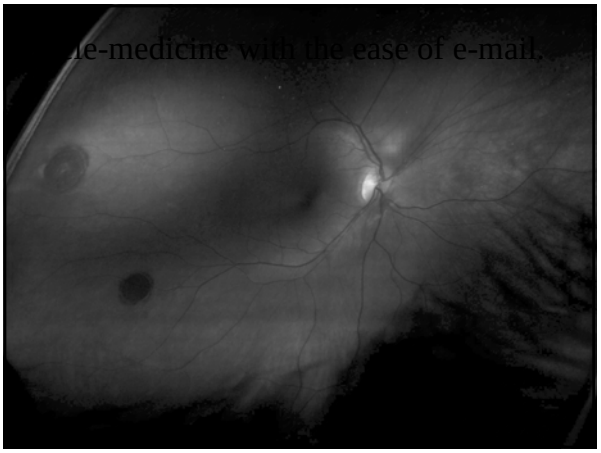


Images taken 8 weeks apart.

Diabetic retinopathy evolves over a short period of time





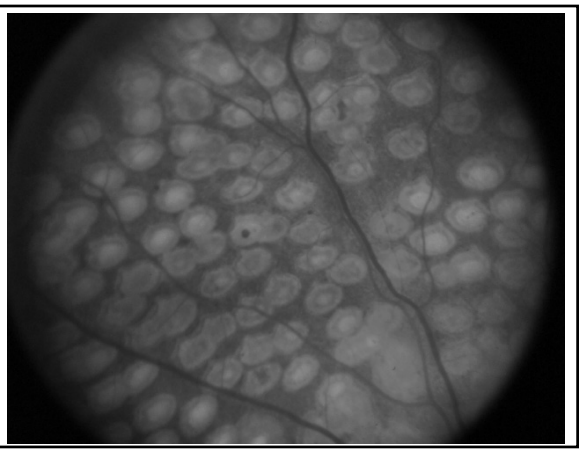
Medical Management

Intensive blood glucose control:
- Oral medications
- Insulin

Anti-hypertensives

Ocular Management

Eye examinations
Laser
Intravitreal Kenalog (steroid)
Cataract surgery
Vitrectomy
Glaucoma filtering surgery



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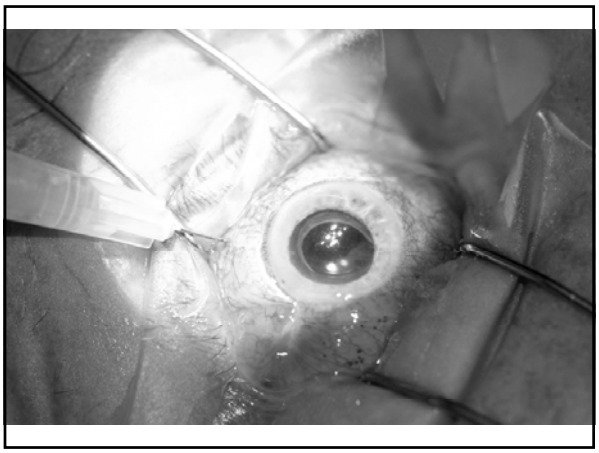
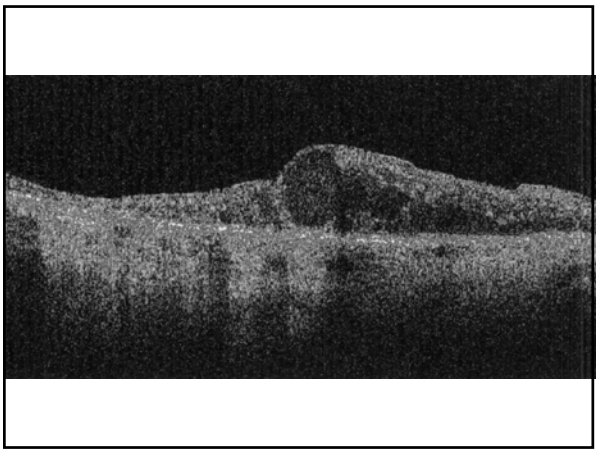
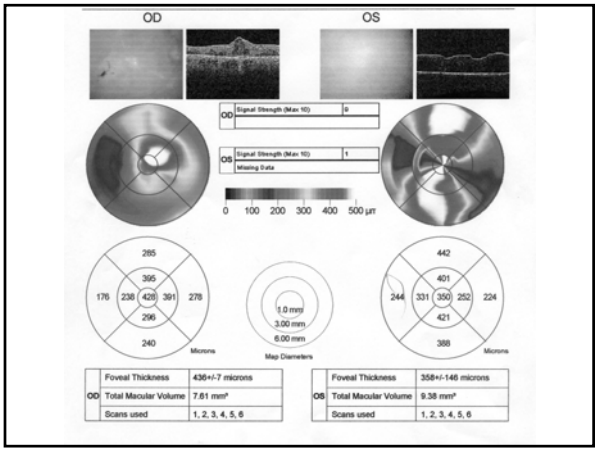
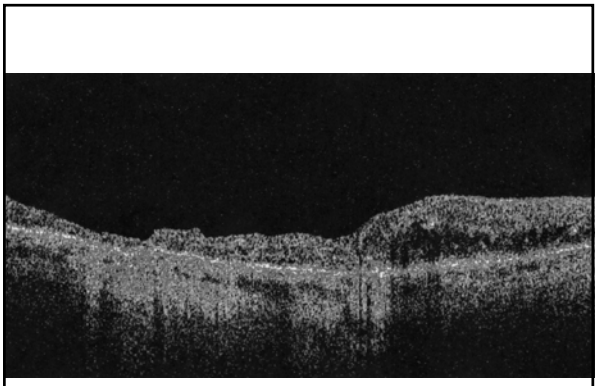
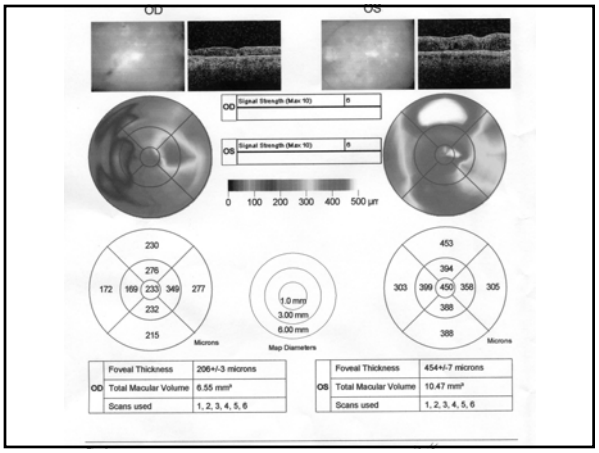








2-3 months later



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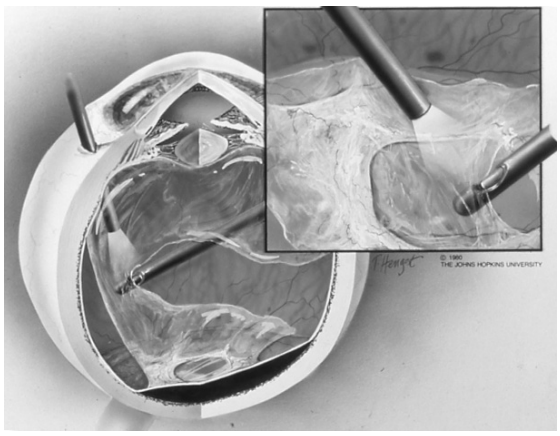
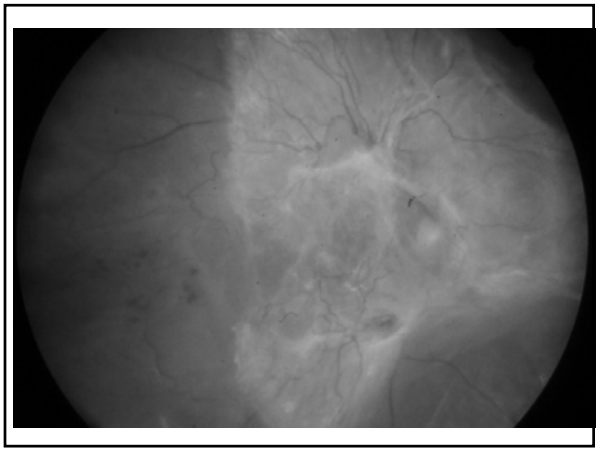
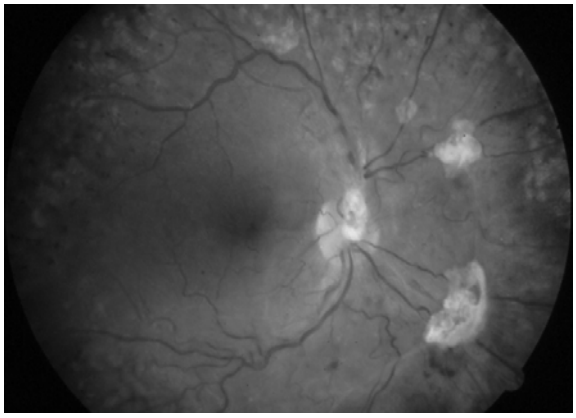
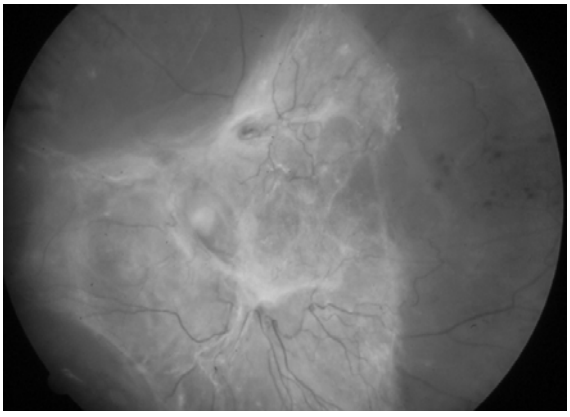
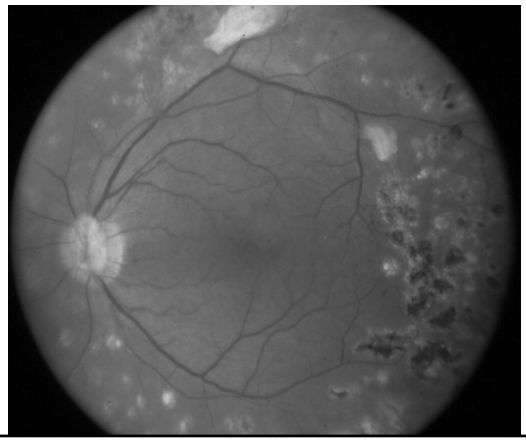


Video
20g Vitrectomy









Studies

Pituitary Ablation Studies
Diabetic Retinopathy Study
Diabetic Retinopathy Vitrectomy Study
Early Treatment Diabetic Retinopathy Study
Diabetes Control and Complication Trial
United Kingdom Prospective Diabetes Study
DRCR

Diabetic Retinopathy Study (DRS)

Is xenon arc and argon laser photocoagulation effective for severe nonproliferative diabetic retinopathy (NPDR) and PDR?

20/100 or better with severe NPDR in both eyes or PDR (active) in one eye.

Randomized to laser or indefinite deferral.

Diabetic Retinopathy Study (DRS)

Is xenon arc and argon laser photocoagulation effective for severe nonproliferative diabetic retinopathy (NPDR) and PDR?

50% reduction in severe vision loss (5/200) over 5 years.

Diabetic Retinopathy Study (DRS)

Four high-risk characteristics (HRCs) identified:

1. Presence of VH or preretinal hemorrhage
2. Presence of neovascularization
3. Presence of neovascularization on or within one disc diameter of disc.
4. Moderate or severe NVD (NVD > ⅓ of disc area or NVE > ½ disc area.

Diabetic Retinopathy Study (DRS)

3 or more HRCs = PRP

2 or less HRCs = still benefit from PRP, but 2-year risk of severe visual loss without treatment was so small that risk of treatment outweigh benefit.

Argon safer than xenon arc.

Diabetic Retinopathy Vitrectomy Study (DRVS)

Is early vitrectomy preferable to deferral when vitreous hemorrhage or very severe PDR is present?

Entry: Recent VH reducing acuity to 5/200 or less for at least one month.

Randomized: PPV 1-6 months or at 12 months

Diabetic Retinopathy Vitrectomy Study (DRVS)

Is early vitrectomy preferable to deferral when vitreous hemorrhage or very severe PDR is present?

Early vitrectomy improves outcomes.

Caveat: Studied over 20 years ago. We now have improved surgical techniques.

Diabetic Retinopathy Vitrectomy Study (DRVS)

Better visual outcomes.

Better anatomic results.

Long-term benefit most apparent with Type I.

Advantage increases with increasing severity.

Early Treatment Diabetic Retinopathy Study (ETDRS)

Evaluated photocoagulation and aspirin treatment patients with NPDR and early PDR.

Early Treatment Diabetic Retinopathy Study (ETDRS)

Thickening at or within 500 microns of FAZ.

Hard exudates at or within 500 microns of FAZ with associated thickening of adjacent retina.

A zone of retinal thickening one disc area or larger, any part of which is within one disc diameter of the center of the macula.

Early Treatment Diabetic Retinopathy Study (ETDRS)

Immediate or delayed focal laser.

Immediate or delayed scatter laser.

ASA 650 mg/day

Early Treatment Diabetic Retinopathy Study (ETDRS)

CSME = prompt focal argon laser = reduced likelihood of vision loss and increased likelihood of vision gain

Edema not CSME = observation

Focal before scatter (PRP)

Early Treatment Diabetic Retinopathy Study (ETDRS)

Aspirin did not help or hurt and did not increase risk of VH

Diabetes Control and Complication Trial

Will intensive control of blood glucose slow development of diabetic retinopathy? Will it slow progression?

Diabetes Control and Complication Trial

Will intensive control of blood glucose slow development of diabetic retinopathy? Will it slow progression?

76% reduction in development
54% reduction in progression

U.K. Prospective Diabetes Study

For Type II DM will intensive blood glucose management reduce microvascular complications including retinopathy progression?

Will intensive blood pressure control reduce microvascular complications including retinopathy progression?

U.K. Prospective Diabetes Study

For Type II DM will intensive blood glucose management reduce microvascular complications including retinopathy progression? Yes.

Will intensive blood pressure control reduce microvascular complications including retinopathy progression? Yes.

Diabetic Retinopathy Clinical Research Network (DRCR.net)

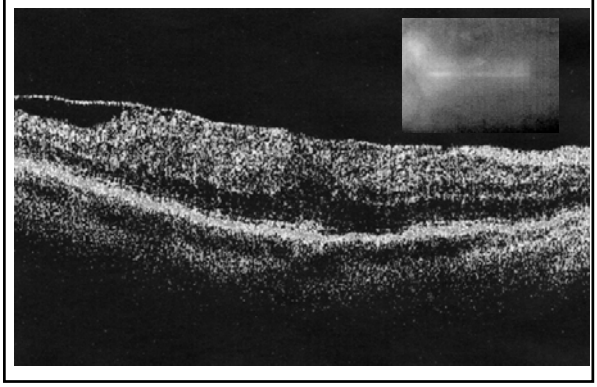
Laser vs. peribulbar triamcinolone for edema

Laser vs. intravitreal triamcinolone for macular edema

Utility of vitrectomy for diabetic macular edema.

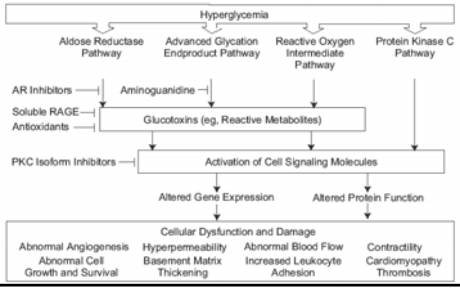
Emerging Therapies

Vitrectomy for CSME
PKC inhibitors
Anti-VEGF (Macugen, Lucentis)
Sustained-release steroid implants (Retisert)



Emerging Therapies

PKC inhibitors: oral agents

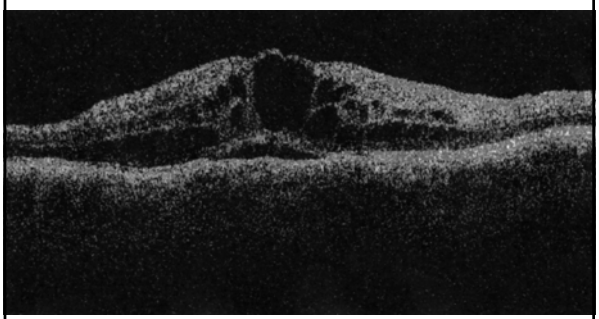


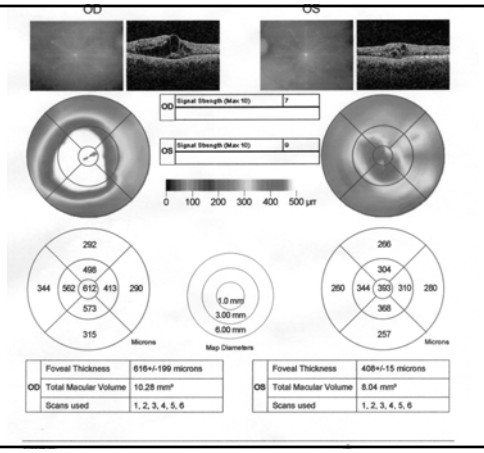
Emerging Therapies

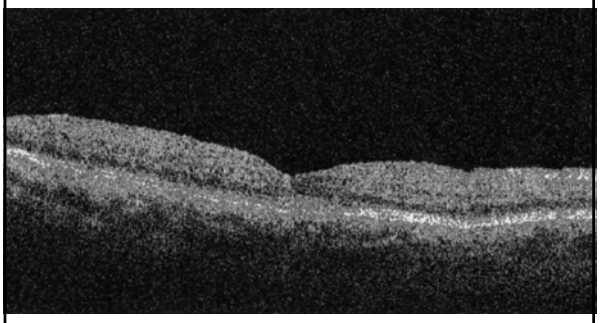
Anti-VEGF (Macugen, Lucentis)

Aptamers bind to VEGF leading to regression of NV and edema.

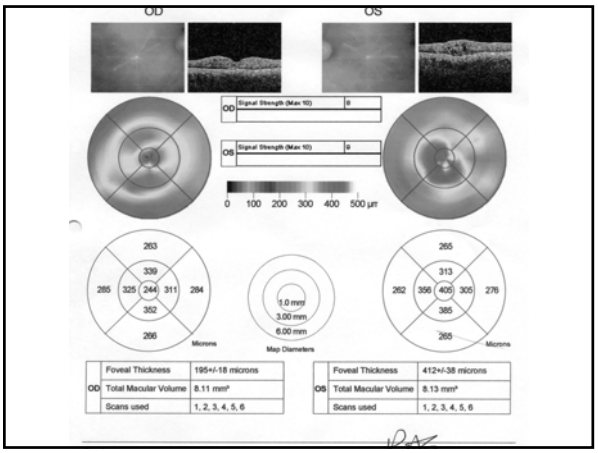
Avastin used off-label currently.
Safe and cost-effective.







4 days later



Emerging Therapies

Sustained-release steroid implants (Retisert) available for uveitis.

$18,000 (orphan drug)
Guarantee of cataract formation
33% develop glaucoma

Emerging Therapies

Improved surgical techniques and instrumentation = less pain and faster recovery.

25 g Video